IN THE CLAIMS:

1-36. (Cancelled)

37. (Currently amended) A method of inhibiting a caspase <u>in vivo</u>, which method comprises:

contacting the caspase with a the compound of the structure:

wherein in Structure I

R¹ is selected from the group consisting of alkyl, substituted alkyl, aryl, and substituted aryl which group -N-CH-(R¹)-(C=O)- will produce a natural amino acid structure or an unnatural amino acid structure, and;

the carbon adjacent to R^1 group is in the D or L configuration; R^2 is selected from the group consisting of

- F; and
$$R^3$$

wherein R³ and R⁴ are each independently selected from the group consisting of hydrogen, alkyl, fluoro, chloro, carboxyl, alkoxy, alkyl carbonyl, aryl carbonyl, and amino; and R⁵ and R⁵ are each independently selected from hydrogen, alkyl, alkoxy, fluoro, chloro, carboxy, alkyl carbonyl, aryl carbonyl, amino and or R⁵ and R⁵ together form a 5 or 6 member carbo cyclic ring structure or a 5 or 6 member heterocyclic ring structure; and

R⁶ is selected from alkyl having 1 to 10 carbon atoms, aryl or substituted aryl;

wherein A is a covalently bonded amine protecting group, and n is 1-4;

$$-O$$
 $-(CH2)n-NH2•X$

wherein X is a salt, and n is 1-4; or

$$-0 \xrightarrow{R'} = 0$$

wherein R⁷ is selected from the group consisting of alkyl having 1 to 10 carbon atoms, aryl and alkylaryl.

38. (Currently amended) A method of inhibiting apoptosis; in vivo, which method comprises

contacting cells containing a caspase: with

(a) a compound of the structure:

wherein in Structure I

R¹ is selected from the group consisting of alkyl, substituted alkyl, aryl, and substituted aryl which group -N-CH (R¹)-(C=O)- will produce a natural amino acid structure or an unnatural amino acid structure, and;

the carbon adjacent to R¹ group is in the D or L configuration; R² is selected from the group consisting of

- F; and
$$-O \longrightarrow \mathbb{R}^3$$

wherein R³ and R⁴ are each independently selected from the group consisting of hydrogen, alkyl, fluoro, chloro, carboxyl, alkoxy, alkyl carbonyl, aryl carbonyl, and amino; and R⁵ and R⁵ are each independently selected from hydrogen, alkyl, alkoxy, fluoro, chloro, carboxy, alkyl carbonyl, aryl carbonyl, amino, and or R⁵ and R⁵ together form a 5 or 6 member carbo cyclic ring structure or a 5 or 6 member heterocyclic ring structure; and

R⁶ is selected from alkyl having 1 to 10 carbon atoms, aryl or substituted aryl;

$$-O$$
 (CH₂)_nNH-A

wherein A is a covalently bonded amine protecting group, and n is 1-4;

$$-O$$
 $-(CH_2)_n$ - NH_2 • X

where X is a salt, and n is 1-4;

$$-0 \xrightarrow{R^7} = 0$$

wherein R⁷ is selected from the group consisting of alkyl having 1 to 10 carbon atoms, aryl and alkylaryl or the acid or base salts thereof.

- 39. (Cancelled)
- 40. (Currently amended) A method inhibition, wherein the method comprises administration to a mammal in need of therapy of:
- (a) a compound of the structure:

wherein in Structure I

 R^1 is selected from the group consisting of alkyl, substituted alkyl, aryl, and substituted aryl which group -N-CH (R^1)-(C=O)- will produce a natural amino acid structure or an unnatural amino acid structure, and;

the carbon adjacent to R^1 group is in the D or L configuration; R^2 is selected from the group consisting of

$$-0$$
 R^3

wherein R³ and R⁴ are each independently selected from the group consisting of hydrogen, alkyl, fluoro, chloro, carboxyl, alkoxy, alkyl carbonyl, aryl carbonyl, and amino; and R⁵ and R⁵ are each independently selected from hydrogen, alkyl, alkoxy, fluoro, chloro, carboxy, alkyl carbonyl, aryl carbonyl, amino, and or R⁵ and R⁵ together form a 5 or 6 member carbo cyclic ring structure or a 5 or 6 member heterocyclic ring structure; and

R⁶ is selected from alkyl having 1 to 10 carbon atoms, aryl or substituted aryl;

$$-O$$
 (CH₂)_nNH-A

wherein A is a covalently bonded amine protecting group, and n is 1-4;

where X is a, and n is 1-4;

$$-0 \xrightarrow{R'} = 0$$

wherein R⁷ is selected from the group consisting of alkyl having 1 to 10 carbon atoms, aryl and alkylaryl or the acid or base salts thereof.

- 41. (Previously presented) The method of Claim 40 wherein in the structure:

 R¹ is selected from isopropyl or isobutyl;

 R² is F; and R⁵ is hydrogen.
- 42. (Original) The method of Claim 40 wherein in the structure: R^1 is selected from isopropyl or isobutyl; R^2 is

$$-0$$
 R^3

wherein R³ and R⁴ are each fluoro; and R⁵ is hydrogen.

- 43. (Previously presented) The method of Claim 42 wherein in the structure, R³ and R⁴ in the 2 and 6 positions of the phenyl ring.
- 44. (Previously presented) The method of Claim 43 wherein R² is

$$-O$$
 $(CH_2)_nNH-A$

45. (Previously presented) The method of Claim 43 wherein R² is

$$-O - (CH2)n-NH2•X$$

46. (Previously presented) The method of Claim 43 wherein R² is

$$-0$$

- 47. (Currently amended) The method of claim 38 wherein the compound comprises,
- (a) a compound of the structure:

wherein R¹ is selected from the group consisting of methyl, ethyl, isopropyl, and iso-butyl;

R² is selected from the group consisting of:

-F or
$$-0$$

wherein R³ and R⁴ are each independently selected from the group consisting of hydrogen, alkyl having 1 to 10 carbon atoms, fluoro, chloro and amino;

and R⁵ and R⁵ are each selected from the group consisting of hydrogen having 1 to 10 carbon atoms, alkyl having 1 to 10 carbon atoms, alkoxyl having 1 to 10 carbon atoms, fluoro, and chloro;

$$-O$$
 $-(CH_2)_n$ -NH₂•X

wherein A is a covalently bonded amine protecting group, and n is 1-4;

wherein X is a salt and n is 1-4;

$$-0$$
 R^7
 $=0$

wherein R⁷ is selected from the group consisting of alkyl having 1 to 10 carbon atoms, aryl and alkylaryl.

48. (Previously presented) The method of Claim 47 wherein R² is

$$-O$$
 (CH₂)_nNH-A

49. (Previously presented) The method of Claim 47 wherein R² is

$$-$$
 O $(CH_2)_n$ -NH₂•X

50. (Previously presented) The method of Claim 47 wherein R² is

$$-0 \xrightarrow{R^{1}} = 0$$

51. (Previously presented) The method of Claim 47, wherein in the structure:

R¹ is selected from isopropyl or iso-butyl;

R² is -F; and

R⁵ is hydrogen.

52. (Previously presented) The method of Claim 47 wherein, in the structure

R¹ is selected from isopropyl or isobutyl;

 R^2 is

$$-0$$
 R^{3}

wherein R³ and R⁴ are each fluoro; and R⁵ is hydrogen.

53. (Previously presented) The method of Claim 47 wherein in the structure, groups R^3 and R^4 are in the 2 and 6 positions of the phenyl ring.

- 54. (Currently amended) A method of Claim 39 for caspase inhibition according to claim 38 wherein inhibitor, which method comprises:
 - (a) a compound is selected from the group consisting of:

; and

55. (Currently amended) A compound of the structure <u>selected from</u>:

m is 1, 2 or 3, creating 1, 2 or 3 amino acid linkages, such that when m = 1, $R^A = R^1$,

when m = 2, R^A is R^1 and R^{1B} in the separate amino acids and

when m = 3, R^A is R^1 , R^{1B} and R^{1C} wherein R^1 , R^{1B} and R^{1C} in the separate amino acids which amino acids are the same or different amino acid when R^1 , R^{1B} and R^{1C} are independently selected from the group consisting of alkyl, substituted alkyl, aryl, and substituted aryl which group -N-CH (R^1)-(C=O)-; N-CH(R^1)-(C=O)-NH-CH(R^{1B})-(C=O); or NCH(R^1)(C=O)-NH-CH(R^{1C})(C=O)- produces natural amino acid structures or an unnatural amino acid structures, and;

the carbon adjacent to R^1 group is in the D or L configuration; R^2 is selected from the group consisting of:

- F; and
$$- O \longrightarrow \mathbb{R}^3$$

wherein R³ and R⁴ are each independently selected from the group consisting of hydrogen, alkyl, fluoro, chloro, carboxyl, alkoxy, alkyl carbonyl, aryl carbonyl, and amino;

and R⁵ and R⁵ are each independently selected from hydrogen, alkyl, alkoxy, fluoro, chloro, carboxy, alkyl carbonyl, aryl carbonyl, amino and or R⁵ and R⁵ together form a 5 or 6 member carbo cyclic ring structure or a 5 or 6 member heterocyclic ring structure; and R⁶ is selected from alkyl having 1 to 10 carbon atoms, aryl or substituted aryl;

$$-O$$
 (CH₂)_nNH-A

wherein A is a covalently bonded amine protecting group, and n is 1-4, preferably 2;

where X is a <u>salt</u>, and n is 1-4, preferably 2; and

$$-0$$

wherein R^7 is selected from the group consisting of alkyl having 1 to 10 carbon atoms, aryl and alkylaryl or the <u>acid</u> or base salts thereof.

- 56. (Previously presented) The compound of Claim 55 wherein m = 2, R^1 and R^{1B} are each independently selected from methyl, ethyl, isopropyl and t-butyl.
 - 57. (Previously presented) The compound of Claim 55 wherein m = 3, R^1 , R^{1B} and

R^{1C} are each independently selected from methyl, ethyl, isopropyl and t-butyl.

- 58. (Previously presented) The compound of Claim 57 wherein R² is F or 2,6-difluorophenoxy, R⁵ and R^{5'} are each hydrogen and R⁶ is methyl.
- 59. (Currently amended) A caspase inhibitor as as a composition comprising:

 a compound selected from the structure: A composition comprising a caspase inhibitor of
 the following structure in combination with a pharmaceutically acceptable carrier,

wherein

m is 1, 2 or 3, creating 1, 2 or 3 amino acid linkages, such that when m = 1, $R^A = R^1$,

when m = 2, R^A is R^1 and R^{1B} in the separate amino acids and

when m = 3, R^A is R^1 , R^{1B} and R^{1C} wherein R^1 , R^{1B} and R^{1C} in the separate amino acids which amino acids are the same or different amino acid when R^1 , R^{1B} and R^{1C} are independently selected from the group consisting of alkyl, substituted alkyl, aryl, and substituted aryl which group -N-CH (R^1)-(C=O)-; N-CH(R^1)-(C=O)-NH-CH(R^{1B})-(C=O); or NCH(R^1)(C=O)-NHCH(R^{1C})(C=O)- produces natural amino acid structures or an unnatural amino acid structures, and;

the carbon adjacent to R¹ group is in the D or L configuration; R² is selected from the group consisting of:

- F; and
$$R^3$$

wherein R³ and R⁴ are each independently selected from the group consisting of hydrogen, alkyl, fluoro, chloro, carboxyl, alkoxy, alkyl carbonyl, aryl carbonyl, and amino; and R⁵ and R⁵ are each independently selected from hydrogen, alkyl, alkoxy, fluoro, chloro, carboxy, alkyl carbonyl, aryl carbonyl, amino and or R⁵ and R⁵ together form a 5 or 6 member carbo cyclic ring structure or a 5 or 6 member heterocyclic ring structure; and

R⁶ is selected from alkyl having 1 to 10 carbon atoms, aryl or substituted aryl;

wherein A is a covalently bonded amine protecting group, and n is 1-4, preferably 2;

where X is a salt, and n is 1-4, preferably 2; and

$$-0$$
 R^{7}
 $=0$

wherein R⁷ is selected from the group consisting of alkyl having 1 to 10 carbon atoms, aryl and alkylaryl or the acid or base salts thereof.

- 60. (Currently amended) The easpase inhibitor composition of Claim 59 wherein m = 2, R^1 and R^{1B} are each independently selected from methyl, ethyl, isopropyl and or t-butyl.
- 61. (Currently amended) The easpase inhibitor composition Claim 59 wherein m = 3, R^1 , R^{1B} and R^{1C} are each independently selected from methyl, ethyl, isopropyl and t-butyl methyl or ethyl.
- 62. (Currently amended) The easpase inhibitor composition Claim 59 wherein R² is F or 2,6-difluorophenoxy, R⁵ and R⁵ are each hydrogen and R⁶ is methyl.
- 63. (Currently amended) The caspase inhibitor composition Claim 62 wherein R^2 is F or 2,6-difluorophenoxy, R^5 and R^5 are each hydrogen and R^6 is methyl.
- 64. (Currently amended) The A method of treatment for a human being diagnosed as having arthritis, septic shock, respiratory diseases, inflammatory condition, cholangitis, colitis, encephalitis, endocerolitis, hepatitis, pancreatitis, reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney disease immune-based diseases, hypersensitivity, multiple sclerosis, bone diseases; and neurodegenerative diseases, Alzheimer's, Amyltrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, and spinal chord injuries which method comprises:
- A. Administering administering an effective amount of the composition caspase inhibitor of claim 59.
- 65. (Currently amended) The A method of treatment of claim 47 of a human being diagnosed as having arthritis, metastases, meningitis, salpingitis, septic shock, respiratory diseases, inflammatory condition, cholangitis, colitis, encephalitis, endocerolitis, hepatitis, pancreatitis, reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney

disease immune based diseases, hypersensitivity, multiple sclerosis, bone diseases; and neurodegenerative diseases, Alzheimer's, Amyltrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, spinal chord injuries and liver damage, traumatic brain injury, which method comprises:

A. Administering administering an effective amount of the composition easpase inhibitor of claim 60.

66. (Currently amended) The A method of treatment of a human being diagnosed as having arthritis, metastases, meningitis, salpingitis, septic shock, respiratory diseases, inflammatory condition, cholangitis, colitis, encephalitis, endocerolitis, hepatitis, pancreatitis, reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney disease immune-based diseases, hypersensitivity, multiple sclerosis, bone diseases; and neurodegenerative diseases, Alzheimer's, Amyltrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, spinal chord injuries and liver damage, traumatic brain injury, alopecia, AIDS and toxin induced liver disease, which method comprises:

A. Administering administering an effective amount of the composition easpase inhibitor of claim 61.

67. (Previously presented) The method of treatment of claim 54 of a human being diagnosed as having arthritis, metastases, meningitis, salpingitis, septic shock, respiratory diseases, inflammatory condition, cholangitis, colitis, encephalitis, endocerolitis, hepatitis, pancreatitis, reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney disease immune based diseases, hypersensitivity, multiple sclerosis, bone diseases; and neurodegenerative diseases, Alzheimer's, Amyltrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, spinal chord injuries and liver damage, traumatic brain injury, alopecia, which method comprises:

A. Administering administering an effective amount of the composition easpase inhibitor of claim 60.

- 68. (Currently amended) The A method of treatment of claim 59 of a human being diagnosed as having arthritis, metastases, meningitis, salpingitis, septic shock, respiratory diseases, inflammatory condition, cholangitis, colitis, encephalitis, endocerolitis, hepatitis, pancreatitis, reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney disease immune based diseases, hypersensitivity, multiple sclerosis, bone diseases; and neurodegenerative diseases, Alzheimer's, Amyltrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, spinal chord injuries and liver damage, and traumatic brain injury, which method comprises:
- A. Administering administering an effective amount of the composition easpase inhibitor of claim 62.
- 69. (Currently amended) The A method of treatment of a human being diagnosed as having arthritis, metastases, meningitis, salpingitis, septic shock, respiratory diseases, inflammatory condition, cholangitis, colitis, encephalitis, endocerolitis, hepatitis, pancreatitis, reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney disease immune based diseases, hypersensitivity, multiple sclerosis, bone diseases; and neurodegenerative diseases, Alzheimer's, Amyltrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, spinal chord injuries and liver damage, and traumatic brain injury, which method comprises:
- A. Administering administering an effective amount of the composition easpase inhibitor of claim 63.
 - 70. (Cancelled)